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Reply

The letter highlights several problems associated with the study of transmyocardial revascularization. Knowledge in diverse technologic and scientific areas is important, ranging from histology and pathology to physics and physiology, and perhaps even history [1]. Additional complications occur because the results of transmyocardial revascularization have changing spatial and temporal components [2]. These inherent complexities are not easy to explain within the constraints of the Journal's Rapid Report format. Therefore, we are grateful to Dr. Beranek for the opportunity to clarify some of the issues arising from our paper [3].

Knowledge of the animal model is crucial to interpretation of the results [4]. Dr. Beranek is mistaken when he states that the normal size of the area at risk (that is, the area of tissue perfused by the occluded artery) in Sprague-Dawley rats is about 70%. In fact, survival would be rare when 70% of the ventricle was ischemic. The size of the area at risk is determined primarily by the site of occlusion of the left coronary artery; the lower the occlusion site, the smaller the area at risk. Nor was this parameter influenced in our experiments by the development of collateral arteries, and the values reported (53 and 55%) are similar to those in studies without transmyocardial revascularization (for example, in Ref. 5; the mean group range was 42–53%). Furthermore, the author states that smaller areas at risk result in smaller areas of necrosis. We found no relationship between infarct size (expressed as a percentage of the area at risk) and area at risk in rat hearts subjected to 90 minutes of occlusion [6]. Infarct size was constant over the entire range of risk areas (20–65%). It is only when the area at risk is small that infarct size is affected; therefore, it is usual to exclude from analysis hearts with areas at risk less than 20%.

We should also correct some misconceptions regarding the histologic methods. The author states that the open channels were not filled with blood and extrapolates this interpretation of our ex vivo micrographs to mean that blood was never there in vivo. The hearts were rinsed in water after they were removed from the chest, incubated in a tetrazolium solution, immersion fixed in formalin, and then processed for paraffin embedding through solutions of alcohol and xylene. These steps resulted in the removal of most red blood cells from the open channels, although some cells were still present.

In addition, sectioning laser-treated hearts presents problems. It is difficult to capture the entire channel length in a single section. To also show the connection to the ventricular cavity and small vessels connecting to the channels requires luck of lottery-winner magnitude. Serial sectioning and subsequent reconstruction is required to appreciate all of these facets [2,7]. The micrographs selected for publication were chosen to illustrate these features separately. Ideally, we would have shown more; however, we have presented micrographs in other publications that lend further support to our conclusions [1,2,4,8,9].

Nevertheless, Dr. Beranek raises some interesting points. The particular collagen fiber organization in scar tissue was an unexpected finding and, as suggested, may be the result of incompletely ablated myocytes providing a framework for subsequent scar collagen alignment and channel closure. We agree that all channels become occluded by thrombus within hours [2]; however, some channels were open months later. There has been no time-course study to examine the natural history of channels made with ultraviolet lasers; therefore, how and why some channels reopen is unknown [2]. In preliminary experiments to determine a suitable laser dose, we found that nonvaporized cells underwent thermally mediated necrosis. As a result, the suggestion that apoptosis is involved in the formation of open channels seems unlikely but should be examined.

It is interesting that Dr. Beranek argues that our hypothesis goes against a "well-established medical paradigm." If anything can be concluded about transmyocardial revascularization, it is that it does not fit well-established paradigms. Whether this is because we lack the knowledge to appreciate the procedure or because it truly represents a "paradigm shift" remains unknown. We encourage examination of our hypotheses and welcome alternative proposals. Only in

this way can transmyocardial revascularization gain acceptance as a legitimate treatment.

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